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10/577,620	01/29/2007	Maria Sitges Berrondo	251989	9639

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EXAMINER
CARTER, KENDRA D

ART UNIT	PAPER NUMBER
1617	

NOTIFICATION DATE	DELIVERY MODE
08/06/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/577,620	SITGES BERRONDO ET AL.	
	Examiner	Art Unit	
	KENDRA D. CARTER	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *4/28/06* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-8 are pending.

Drawings

The drawings are objected to under 37 CFR 1.83(a) because they fail to show what the asterisks stands for. Any structural detail that is essential for a proper understanding of the disclosed invention should be shown in the drawing. MPEP § 608.02(d). Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner,

the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

The disclosure is objected to because of the following informalities: the asterisks in the tables on page 8, 9 and 11 are not described in the specification or the figures. The Examiner does not know what the asterisks stand for or correlate to because they do not seem match the disclosed Figures. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1) Claims 1 and 4-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Particularly, there is no written description for the effective treatment of hearing loss with any specific vinpocetine derivative. The skilled practitioner would have to test each and every derivative of vinpocetine, or at least a subset, to determine treatment efficacy for hearing loss. For example, to test for hearing loss, a particular compound that is able to alter auditory brainstem response waves with or without pentylenetetrazole or 4-aminopyridine, would have to be selected synthesized, and tested in the guinea pig animal model to find a dosage regimen (dose amount, frequency, route of administration). If efficacy of the drug did not result, the dosage regime would have to be varied, for example by changing the dosage amount or route of administration, until efficacy was achieved. Thus, the skilled artisan would have to undergo exhaustive studies to evaluate each derivative of vinpocetine. Thus, there is no written description of effectively treating hearing loss with vinpocetine derivatives.

2) Claim 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for preventing hearing loss in the 4 and 8 kHz tone frequencies associated with epilepsy , does not reasonably provide enablement for completely preventing hearing loss. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant claims are drawn to a method of treting or preventing hearing loss associated with epilepsy comprising administering vinpocetine. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention. Attention is directed to *In re Wands*, 8USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:
(1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The nature of the invention:

The claim 1 is drawn to "a method of treating or preventing hearing loss associated with epilepsy in a patient comprising administering to the patient vinpocetine or a derivative thereof in an amount effective to antagonize alterations in the auditory brainstem response (ABR) waves."

(2) The breadth of the claims:

Claim 1 embraces and reads on completely preventing hearing. The specification does not enable the prevention of hearing loss.

(3) The state of the prior art:

The state of the art regarding preventing hearing loss is very low or do not exist. Nekrassov et al. teach that vinpocetine has protective effects but does not indicate that vinpocetine completely prevent hearing loss (see page 227, column 1, section 4.1). Vinpocetine is given after the administration of AMIKACIN, not before (see page 223, column 1, section 2.1). The normal human's hearing range is from 16 Hz to 16.3 mHz (see Wikipedia, page 1, first paragraph).

(4) The predictability or unpredictability of the art:

The predictability of completely preventing hearing loss is relatively low. Therefore, to one skilled in the art, prevention of hearing loss is highly unpredictable.

(5) The relative skill of those in the art:

The relative skill of those in the art is high.

(6) The amount of direction or guidance presented / working examples:

In the instant case, the guidance of the specification as to the complete prevention of hearing loss is lacking. The specification as filed does not speak on or show any working examples any studies performed that completely prevents hearing loss. Note that lack of a working example, is a critical factor to be considered,

especially in a case involving an unpredictable and undeveloped art. See MPEP 2164.02. The specification teaches that when vinpocetin is pre-injected before the convulsing agent is administered, the animas do not have hearing loss in the 4 and 8 kHz tone frequencies (see page 8, paragraph 35 and the table on page 9). The specification does not provide this effect is in all, or a larger subset or hearing frequencies. Thus, hearing loss may occur, but not in the 4 and 8 kHz tone frequencies. As Wikipedia teaches, the normal human's hearing range is from 16 Hz to 16.3 mHz

(7) The quantity of experimentation necessary:

The instant claims read on the completely preventing hearing loss. As discussed above the specification fails to provide any support for completely preventing hearing loss. Applicant fails to provide any information sufficient to practice the claimed invention, absent undue experimentation. Genetech, 108 F. 3d at 1366 states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimation of general ideas that may or may not be workable. Since only the 4 and 8kHz tone frequencies were tested, one can not assume that there is no hearing loss in the other frequencies (i.e. 16 Hz to 3kHz). The tone frequencies tested to not provide a good representation of the frequencies that a normal human hears.

In conclusion, the applicant is enabled for treating and preventing hearing loss associated with epilepsy at 4 and 8 kHz, but not for completely preventing hearing loss.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nekrassov et al. (Brain Research, 2000, vol. 868, pp. 222-229) in view of Holtz et al. (Eur. Arch Otorhinolaryngol, 1990, vol 247, pp. 202-205)..

Nekrassov et al. teach vinpocetine protects from aminoglycoside antibiotic-induced hearing loss in guinea pig in vivo (see title). Amikacin, the aminoglycoside antibiotic, increases the auditory brainstem response (ABR) at 4 and 8 kHz, but when vinpocetine is administed by i.p. at 2 mg/kg for 13 days after administration of Amikacin, the increase ABR threshold is reduced (see abstract and page 225, section 3.5; addresses claims 1, 2 and 4-8).

Nekrassov et al. do not teach that the hearing loss is associated with epilepsy (claim 1), nor the specific treatment of alterations of retro-cochlear origin characterized by the inhibition of the alterations of the ABR (claim 2). Nekrassov et al. also does not specifically teach the the increase in the auditory threshold is induced by pentylenetetrazole or 4-aminopyridine (claim 3). Nekrassov et al. also does not specifically teach vinpocetine is in an amount effective to inhibit the epileptic cortical activity for ictal and post-ictal periods (claim 4).

Holtz et al. teach that aminoglycoside therapy causes cochlear and retrocochlear changes in the auditory pathways (see page 205, column 1, lines 2-5).

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the teachings of Nekrassov et al. and that the hearing loss is associated with epilepsy as in claim 1 because Nekrassov et al. teach the treatment and prevention of hearing loss at 4 and 8 kHz with the Applicant's claimed

compound. Thus, regardless of the cause, hearing loss is still treated. One would be motivated to try a treatment for hearing loss regardless of its cause, especially if the hearing loss was treated.

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the teachings of Nekrassov et al. and treatment of alterations of retro-cochlear origin characterized by the inhibition of the alterations of the ABR (claims 2 and 3) because Nekrassov et al. teach that the ABR waves were inhibited by the same compound. Further, Holtz et al. teach that aminoglycoside therapy causes retro-cochlear changes in auditory pathways. Thus, the treatment of Nekrassov et al. is treating alterations of retro-cochlear origin characterized by the inhibition of the alterations of the amplitudes and latencies of the later waves of the ABR.

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the teachings of Nekrassov et al. and wherein the auditory threshold was induced by pentylenetetrazole or 4-aminopyridine because Holtz et al. teaches that aminoglycoside therapy causes retrocochlear changes in the auitory pathway. Thus, the hearing loss treated by Nekrassov et al. is hearing loss of retro-cochlear origin. Since pentylenetetrazole, 4-aminopyridine and aminoglycoside therapy all increase the auditory threshold and are of retro-cochlear origin it would be obvious to

treat them with the same compound that was shown to be successful in treating the hearing loss as taught by Nekrassov et al.

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the teachings of Nekrassov et al. and that vinpocetine is in an amount effective to inhibit the epileptic cortical activity for ictal and post-ictal periods (claim 4) because Nekrossov et al. teach that vinpocetine was administered at 2 mg/kg, which is the effective amount disclosed in the specification (see page 5, paragraph 23, last line). Thus, the same compound at the same amount would be in an effective amount to inhibit the epileptic cortical activity for ictal and post-ictal periods.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KENDRA D. CARTER whose telephone number is (571)272-9034. The examiner can normally be reached on 7:30 am - 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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